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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,696	12/03/2003	Chaitan Khosla	300622000508	8649
25225	7590	09/23/2008	EXAMINER	
MORRISON & FOERSTER LLP			KIM, ALEXANDER D	
12531 HIGH BLUFF DRIVE			ART UNIT	PAPER NUMBER
SUITE 100			1656	
SAN DIEGO, CA 92130-2040			MAIL DATE	DELIVERY MODE
			09/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/727,696

Applicant(s)

KHOSLA ET AL.

Examiner

ALEXANDER D. KIM

Art Unit

1656

—The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

THE REPLY FILED 08 September 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires ____ months from the mailing date of the final rejection.
 b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
 Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) They raise the issue of new matter (see NOTE below);
 (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. Applicant's reply has overcome the following rejection(s): _____.

6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: 1-5, 7, 10-13 and 31.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fail to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet

12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____

13. Other: _____.

/Chih-Min Kam/
Primary Examiner, Art Unit 1656

Continuation of 11. does NOT place the application in condition for allowance because: The request for reconsideration in the reply filed on 09/08/2008 has been considered, however, the amendment does not place the application in condition for allowance. The amendment to the claims filed on 09/08/2008 has been entered because the claims as amended does not raise new issues. However, in view of the entry of the amendment, applicant's arguments are not found persuasive to overcome the outstanding rejection(s) as set forth in the Office action mailed on 07/09/2008 for the reasons of record stated herein. Applicants argue that there is no case law addressing the issue of whether substituting "consists of" or "comprises" constitutes new matter and traverse since said amendment limits the claims only to those elements that is disclosed. However, the instant application does not disclose method having only two steps, i.e., excising a nucleotide sequence and ligating into a second nucleotide sequence, as if the novelty of instant invention is a method involving novel step of modifying DNA sequence(s). The instant application disclose, but not limited to, the method comprising at least steps of preparing a cosmid library of genomic DNA from *Streptomyces hygroscopicus*, excising and ligating a nucleotide sequence of interest to another nucleotide sequence, transforming into *S. coelicolor* using expression vector, manipulating macrolide ring size by mutagenesis using the expression system of Kao et al., wherein said step is different from method step as claimed in Claim 1 (Claims 2-5 and 31 dependent therefrom). Instant claimed invention having just two step of excising and ligating an AT domain to a second AT domain is not supported by the original disclosure. Thus, the previous new matter rejection under 35 USC 112 would be maintained. If Applicants argue that instant invention of having excising and ligating step within the application's disclosure supports the instant claim 1 by just looking at step of excising and ligating step, and not considering all the other step that is also recited in the original disclosure, then the previous rejections under 35 USC 102 and 103 (which were withdrawn) would be a proper rejection by the same analogy that is just considering steps taught by Katz et al. disclosing steps consider to be excising and ligating nucleotide sequences. Furthermore, Applicants also acknowledge that "Kao does teach such techniques" (see page 6, line 19, Remarks filed on 9/8/2008) would be considered for a prior art.

Applicants also traverse the previous 35 USC 103 rejection. Applicants argue that the previous remarks stating that Kao is irrelevant to these claims" clearly refers to claims 1-5 and 31, not to claims 7 and 10-13. The examiner acknowledge that the argument was made for traversal of Claims 1-5 and 31. Applicants also stated that applicants do not understand the recitation of page 6, lines 26-29 of the Katz PCT publication. However, as disclosed in the previous final rejection mailed on 7/9/2008, the recitation of page 6, lines 26-29 was referring to page of previous non-final rejection mailed on 10/26/2007).

Applicants acknowledge that claims 7 describe a variant of the method described by Kao as applied to exchanging an AT segment of a polyketide synthase-encoding sequence. However, the challenges in doing so are much greater because the flanking sequence that must be used to exchange just this segment must be matched in the donor and acceptor plasmids. Applicants argue that these regions are derived from different polyketide synthases and are assumed to be essential for the function of the synthases involved. However, method of instant claims is not limited to any specific and/or essential sequences as alleged by applicants. Thus, as previously noted, Claims 7 and 10-13 are unpatentable over by Katz (WO 93/13663) or U. S. P 5,824,513 ('513, IDS reference number 5) in view of the state of the art as exemplified by Kao et al. (IDS reference: Science 1994, 265, 509-512)..